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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,431	03/25/2005	Gregoire Prevost	117P/PCT2/US	6671

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EXAMINER	
OLSON, ERIC	
ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,431	PREVOST ET AL.	
	Examiner	Art Unit	
	ERIC S. OLSON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Februaryt 23, 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,22,26,31 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,22,26,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 23, 2009 has been entered.

Detailed Action

This office action is a response to applicant's communication submitted February 23, 2009 wherein claims 17, 22, and 26 are amended and claims 18 and 19 are cancelled. This application is a national stage application of PCT/IB03/04922, filed September 29, 2003, which claims benefit of provisional application 60/414103, filed September 27, 2002.

Claims 17, 22, 26, 31, and 32 are pending in this application.

Claims 17, 22, 26, 31, and 32 as amended are examined on the merits herein.

The following new grounds of rejection are introduced:

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17, 22, 26, 31, and 32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11, 13, 17, 21, and 24-26 of copending Application No. 12/073729. (Published as pre-grant publication 2008/0161253, cited in PTO-892, herein referred to as '729) Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 11, 13, 17, 21, and 24-26 of '729 anticipate the claimed invention.

Claim 11 of '729 discloses a pharmaceutical composition comprising the specific compound recited in instant claim 17 and an anthracycline. Claim 13 claims a composition wherein the anthracycline is doxorubicin. Claims 17 and 21 of '729 claim methods of decreasing the rate of proliferation of nasopharyngeal carcinoma cells or of treating nasopharyngeal carcinoma comprising administering the compositions comprising the claimed compound and doxorubicin. Claims 24-26 of '729 further disclose a method wherein the subject is a mammal or a human. Therefore claims 11, 13, 17, 21, and 24-26 of '729 anticipate the claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following rejections of record in the previous action are maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gordon et al. (PCT international publication WO00/39130, of record in the previous office action) in view of Rybak. (PCT international publication WO01/64197, of record in the previous office action)

Gordon et al. discloses a pharmaceutical composition comprising one of a variety of compounds having an identical formula to formula (I) recited in instant claim 2. (pp. 2-9) Further specifically recited embodiments include the farnesyl transferase inhibitors of instant claims 3-17. (pp. 17-27) These compounds are disclosed to possess anti-tumor activity (p. 16, lines 16-29) and to be useful for inhibiting prenyl transferases including farnesyl transferase. (p. 9, lines 8-25) Gordon et al. does not disclose a pharmaceutical composition comprising a combination of compound according to structure (I) and an anthracycline, or a method of treating nasopharyngeal cancer by administering such a

composition to a subject. Gordon et al. also does not disclose a pharmaceutical kit comprising such a composition according to instant claims 34 and 38.

Rybak discloses therapeutic combinations of anthracyclines and farnesyl transferase inhibitors which are effective in the inhibition of tumor cell growth. (p. 13, lines 3-6) Preferred anthracycline derivatives include daunorubicin, doxorubicin, and idarubicin. (p. 21, lines 24-26) These compositions may be used in a method of inhibiting abnormal cell growth or treating various cancers having aberrant or mutated *ras* oncogene, (p. 22, lines 12-38) in a mammal, particularly a human. The two components may be administered either simultaneously or sequentially. (p. 23, lines 16-18)

It would have been obvious to one of ordinary skill in the art at the time of the invention to produce a pharmaceutical composition comprising a farnesyl transferase inhibitor according to Gordon et al. and further comprising an anthracycline such as doxorubicin. One of ordinary skill in the art would have been motivated to combine the two components and to administer them to a patient suffering from cancer because both components were known to be useful for the treatment of cancer. One of ordinary skill in the art would have reasonably expected success because both compounds were known to be useful for the same purpose. It has been held that it is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose in order to practice a third composition for the very same purpose. The idea of combining them flows logically from their having been taught individually in the prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, submitted February 23, 2009, with respect to the above ground of rejection, have been fully considered and not found to be persuasive to remove the rejection. Applicant argues that the cited references do not give any reason to single out this specific combination of the claimed inhibitor with doxorubicin. However, Gordon et al. discloses a list of merely 40 compounds as examples of specific compounds useful in the invention, one of which is the claimed compound of instant claim 17. Thus one of ordinary skill in the art would merely have to select this compound for use as the farnesyl transferase inhibitor in the compositions and methods described by Rybak.

Applicant further quotes *Takeda Chemical vs. Alphapharm* to establish that when the prior art "disclosed a broad selection of compounds any one of which could have been selected as a lead compound for further investigation," it would not have been obvious to one of ordinary skill in the art to select the particular compound for further modification. However, the facts of *Takeda* differ from those of the instant case.

Firstly, *Takeda* concerned a compound which was not disclosed in the cited prior art. Rather, the prior art disclosed a similar compound of similar structure (compound b in patent '477) which differed from the claimed compound by homologation and ring walking of an alkyl group attached to an aromatic ring. Thus one of ordinary skill in the art would have to not only select the specific compound from the prior art but also chemically modify it to arrive at the claimed invention. By contrast, in the instant case, one of ordinary skill in the art needs merely to select the compound and use it as

pictured in the prior art reference Gordon et al. without any further chemical modification.

Secondly, the court in *Takeda* considered several sources of secondary evidence in making its decision. A prior art publication (the Sodha II reference) disclosed significant negative properties associated with the alleged lead compound b relied on in the rationale for obviousness, thus teaching away from using compound b as a lead compound. Furthermore two witnesses testified that the compound b would not have been considered as a promising lead compound at the time of invention due to its adverse affects. Finally, these adverse affects were unexpectedly absent in the claimed compound at issue in *Takeda*, providing evidence of nonobviousness. Therefore the conclusion in *Takeda* depended on the presence of secondary factors that are not present in the instant case.

Essentially, in the fact pattern of *Takeda*, one of ordinary skill in the art would have to make two steps to arrive at the claimed invention:

A) Selecting the prior art compound as a lead compound **even though it had been described as an inferior compound to several related antidiabetic compounds**.

B) Modifying the prior art compound **by altering its chemical structure**.

By contrast, in the instant case, the steps taken by one of ordinary skill in the art are as follows:

A) Selecting the claimed compound from a number of compounds disclosed to be equally pertinent to the treatment of cancer.

B) Using this compound without any further chemical modification in an anticancer method in place of another compound having the exact same biological activity. (ras inhibition)

Thus the steps taken by one of ordinary skill in the art in the instant case to practice the claimed invention are much less radical and more predictable than those necessary in the situation described in *Takeda*. As a result, Applicant's arguments concerning the conclusion in *Takeda* are not seen to be persuasive to remove the rejection.

For these reasons the rejection is maintained.

Claims 22, 26, 31, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gordon et al. (PCT international publication WO00/39130, of record in the previous office action) in view of Rybak. (PCT international publication WO01/64197, of record in the previous office action) as applied to claims 17-19 above, and further in view of Porter et al. (Reference of record in previous action)

The disclosure of Gordon et al. in view of Rybak is discussed above. Gordon et al. in view of Rybak does not disclose a method of treating nasopharyngeal carcinoma in particular.

Porter et al. discloses a study of the expression of certain oncogenes in nasopharyngeal carcinoma. (p. 105, left column, paragraphs 2-3) 73% of nasopharyngeal carcinomas studies were seen to have moderate or intense *ras* expression. (p. 106, right column, table I)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the compositions and methods of Gordon et al. in view of Rybak to treat nasopharyngeal carcinomas such as those of Porter et al. that express the *ras* oncogene. One of ordinary skill in the art would have been motivated to treat these cancers because Rybak already discloses that the combination of a FT inhibitor and an anthracycline is useful for treating cancers that express the *ras* oncogene, and Porter et al. discloses that many nasopharyngeal carcinomas fall within this category. One of ordinary skill in the art would reasonably have expected success because testing a tumor to determine whether a particular oncogene is expressed is well within the ordinary and routine level of skill in the art.

Therefore the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's arguments, submitted August 27, 2008, with respect to the above ground of rejection, have been fully considered and not found to be persuasive to remove the rejection. Applicant's arguments are the same as those made with respect to the above ground of rejection in view of Gordon et al. and Rybak et al. alone.

Applicant further argues that the prior art does not specifically teach that *ras* activity is the key to the effectiveness of combinations of FTA and doxorubicin against

certain tumors. However, p. 22, lines 12-38 of Rybak et al. clearly identifies the target cells of FTI/doxorubicin therapy as being tumor cells expression an abnormal *ras* gene or protein. Because anthracyclines are a required element of the inventive combination of Rybak, one of ordinary skill in the art would have considered this teaching to be a disclosure that the combination of these two agents is effective against *ras*-mediated tumors. This is enough for one of ordinary skill in the art to reasonably expect that using a combination of a FTI and doxorubicin will inhibit these cancer cells.

For these reasons the rejection is deemed proper and maintained.

Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. OLSON whose telephone number is (571)272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/
Examiner, Art Unit 1623
5/14/2009